Figure 1A.

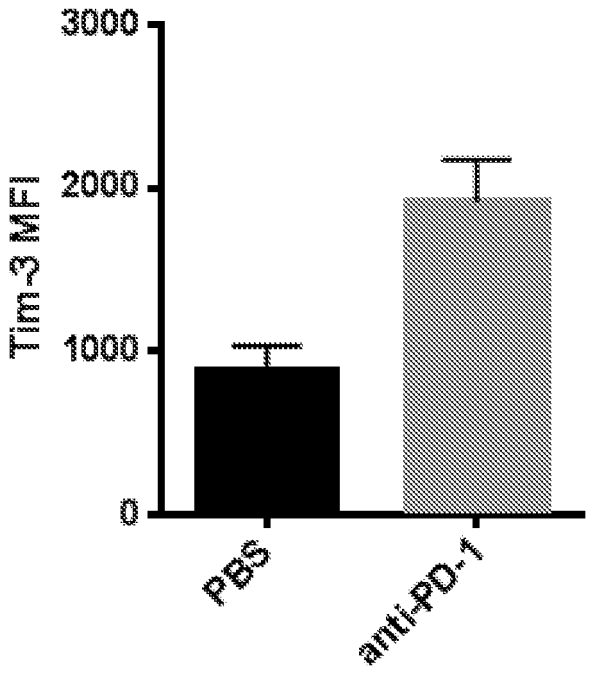


Figure 1B.

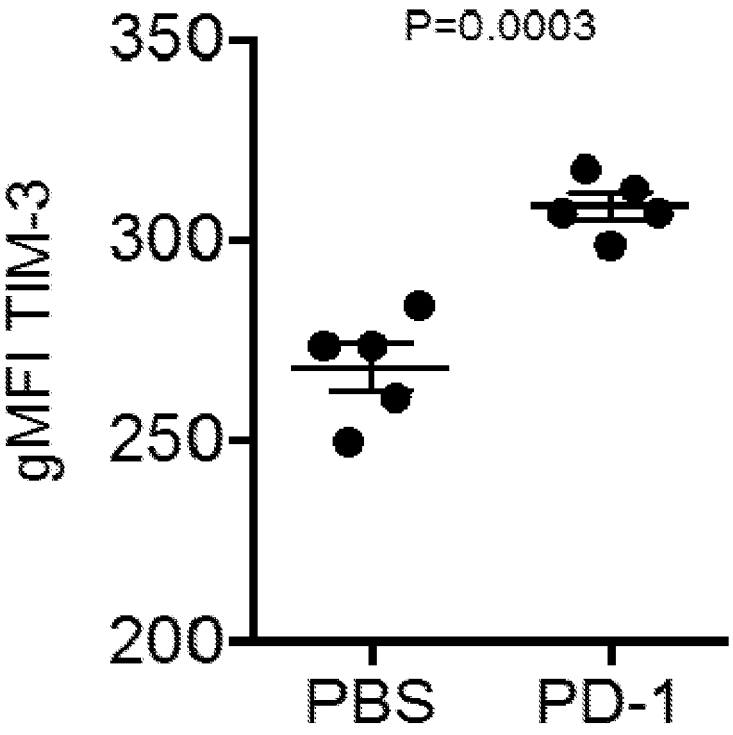


Figure 1C.

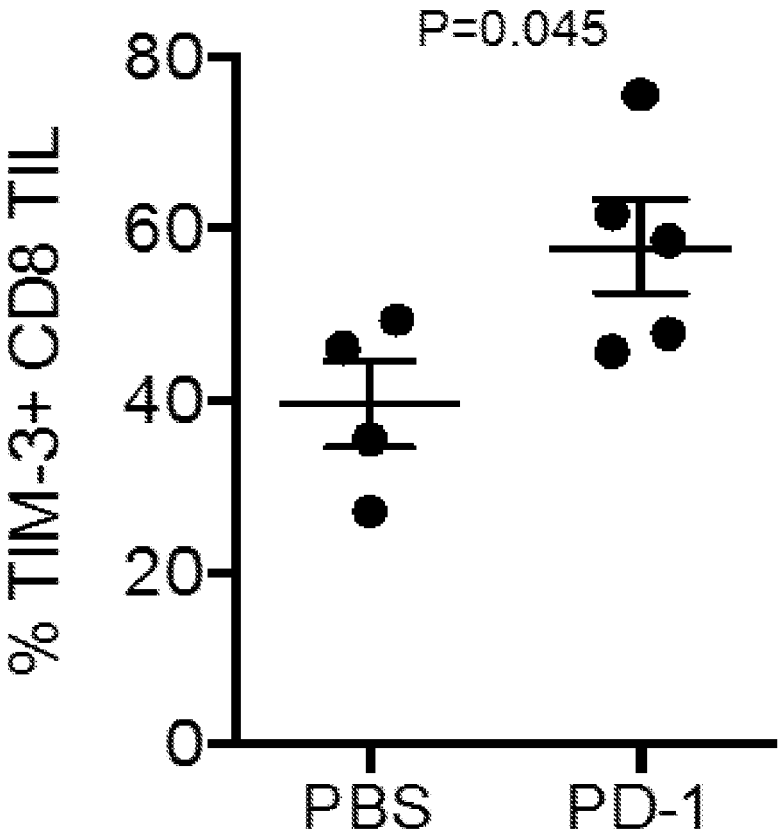


Figure 2A.

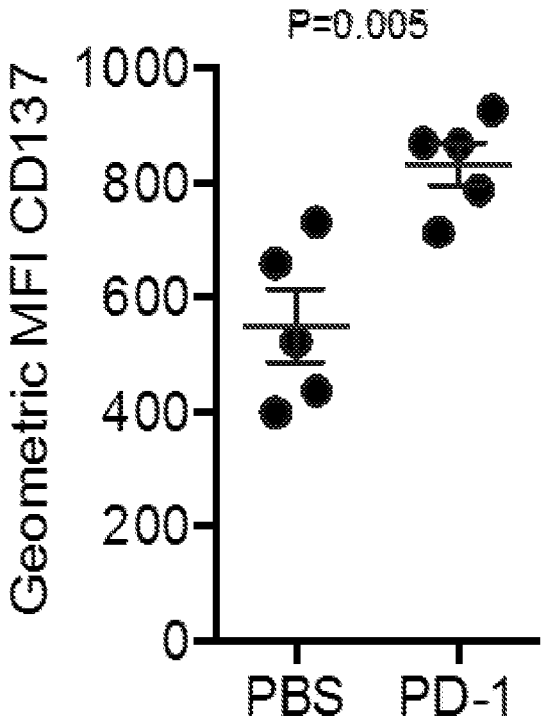


Figure 2B.

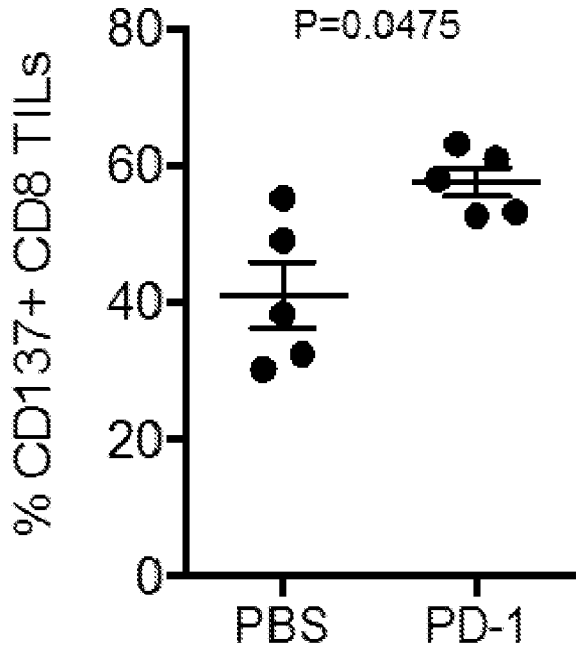


Figure 3A.

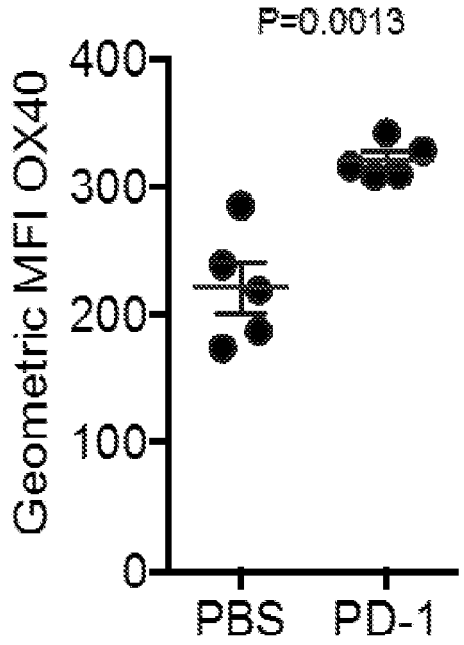


Figure 3B.

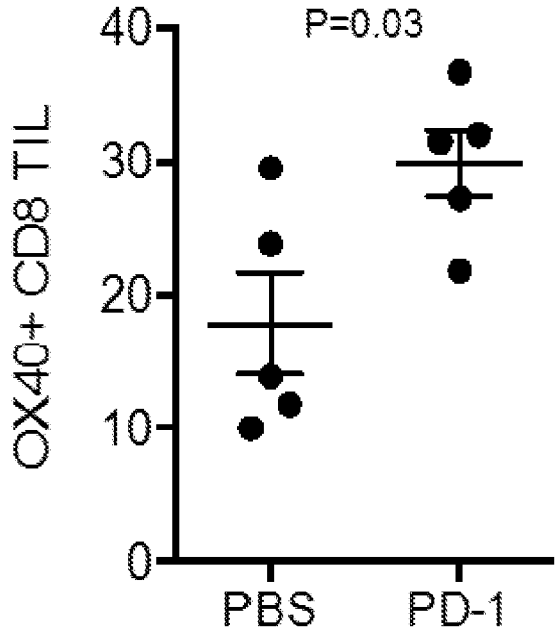


Figure 4A.

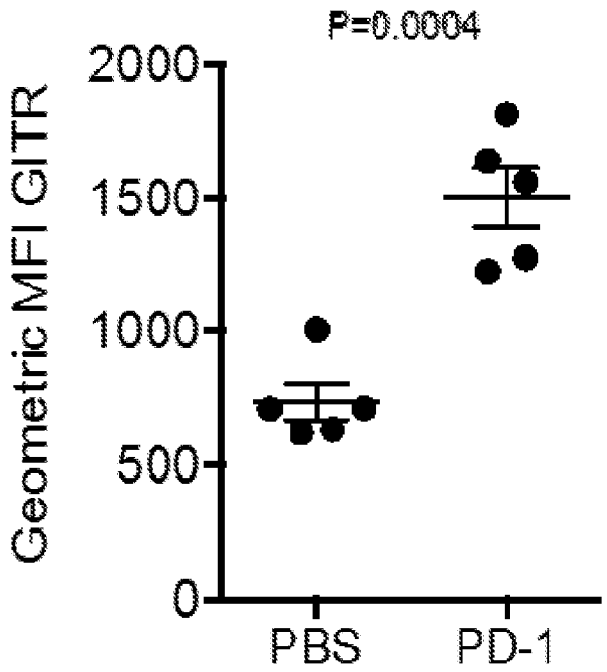


Figure 4B.

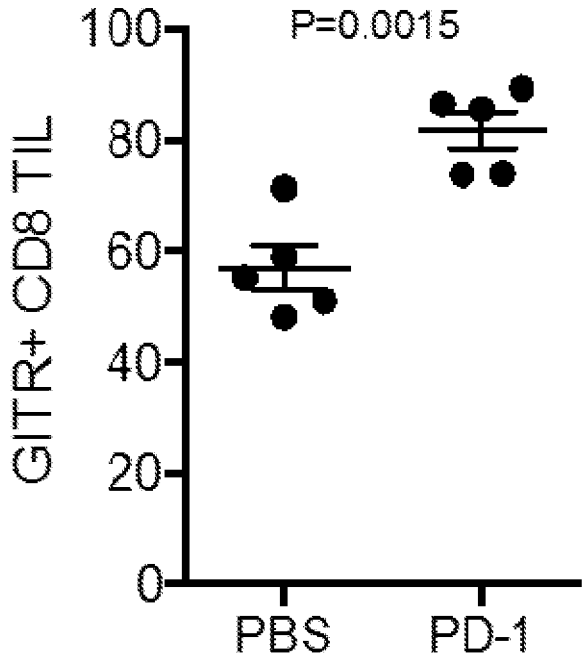


Figure 5.

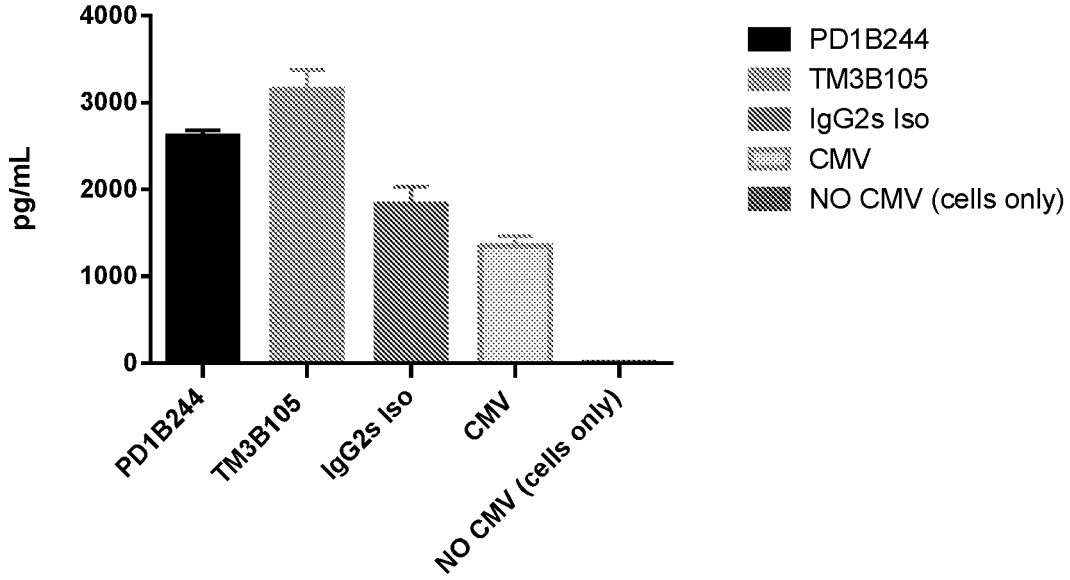

4000
3000
2000
1000
0
pg/mL
PD1B244
TM3B105
IgG2s Iso
CMV
NO CMV (cells only)
PD1B244
TM3B105
IgG2s Iso
CMV
NO CMV (cells only)

Figure 6.

Antibody	HCDR1					
	Sequence					SEQ ID NO:
PD1B114	S	Y	A	I	S	10
PD1B149	S	Y	A	I	S	10
PD1B160	S	Y	A	I	S	10
PD1B162	S	Y	A	I	S	10
PD1B164	S	Y	A	I	S	10
PD1B11	S	Y	A	I	S	10
PD1B183	S	Y	A	I	S	10
PD1B184	S	Y	A	I	S	10
PD1B185	S	Y	A	I	S	10
PD1B187	S	Y	A	I	S	10
PD1B71	S	Y	A	I	S	10
PD1B177	D	Y	V	I	S	11
PD1B70	S	Y	A	I	S	10
PD1B175	S	Y	V	I	H	12
PD1B194	S	Y	A	I	S	10
PD1B195	S	Y	A	I	S	10
PD1B196	S	Y	A	I	S	10
PD1B197	S	Y	V	I	H	12
PD1B198	S	Y	V	I	H	12
PD1B199	D	Y	V	I	S	11
PD1B200	D	Y	V	I	S	11
PD1B201	D	Y	V	I	S	11
HCDR1 genus	X_1	Y	X_2	I	X_3	82

PD-1 mAb HCDR1 genus sequence:

$X_1YX_2IX_3$ (SEQ ID NO: 82),

wherein

X_1 is S or D;

X_2 is V or A; and

X_3 is H or S.

Figure 7.

Antibody	HCDR2																	
	Sequence																	SEQ ID NO:
PD1B114	G	I	I	P	I	F	G	T	A	N	Y	A	Q	K	F	Q	G	13
PD1B149	G	I	I	P	I	F	G	T	A	N	Y	A	Q	K	F	Q	G	13
PD1B160	G	I	I	P	I	F	D	T	A	N	Y	A	Q	K	F	Q	G	14
PD1B162	G	I	I	P	I	F	D	T	A	N	Y	A	Q	K	F	Q	G	14
PD1B164	G	I	I	P	I	F	D	T	A	N	Y	A	Q	K	F	Q	G	14
PD1B11	G	I	I	P	I	F	G	T	A	N	Y	A	Q	K	F	Q	G	13
PD1B183	G	I	I	P	I	F	G	T	A	N	Y	A	Q	K	F	Q	G	13
PD1B184	G	I	I	P	I	F	G	T	A	N	Y	A	Q	K	F	Q	G	13
PD1B185	G	I	I	P	I	F	G	T	A	N	Y	A	Q	K	F	Q	G	13
PD1B187	G	I	I	P	I	F	G	T	A	N	Y	A	Q	K	F	Q	G	13
PD1B71	G	I	I	P	I	F	G	T	A	N	Y	A	Q	K	F	Q	G	13
PD1B177	G	I	I	P	I	Y	G	T	A	N	Y	A	Q	K	F	Q	G	15
PD1B70	G	I	I	P	I	F	G	T	A	N	Y	A	Q	K	F	Q	G	13
PD1B175	G	I	I	P	I	F	G	T	A	N	Y	A	Q	K	F	Q	G	13
PD1B194	G	I	I	P	I	F	D	T	A	N	Y	A	Q	K	F	Q	G	14
PD1B195	G	I	I	P	I	F	D	T	A	N	Y	A	Q	K	F	Q	G	14
PD1B196	G	I	I	P	I	F	D	T	A	N	Y	A	Q	K	F	Q	G	14
PD1B197	G	I	I	P	I	F	G	T	A	N	Y	A	Q	K	F	Q	G	13
PD1B198	G	I	I	P	I	F	G	T	A	N	Y	A	Q	K	F	Q	G	13
PD1B199	G	I	I	P	I	Y	G	T	A	N	Y	A	Q	K	F	Q	G	15
PD1B200	G	I	I	P	I	Y	G	T	A	N	Y	A	Q	K	F	Q	G	15
PD1B201	G	I	I	P	I	Y	G	T	A	N	Y	A	Q	K	F	Q	G	15
HCDR2 genus	G	I	I	P	I	X_4	X_5	T	A	N	Y	A	Q	K	F	Q	G	83

PD-1 mAb HCDR2 genus sequence

GIIPIX_4X_5TANYAQKFQG (SEQ ID NO: 83),

wherein

X_4 is Y or F; and

X_5 is G or D.

Figure 8.

Antibody	HCDR3														
	Sequence														SEQ ID NO:
PD1B114	P	G	L	A	A	A	Y	D	T	G	N	L	D	Y	16
PD1B149	P	G	L	A	A	A	Y	D	T	G	N	L	D	Y	16
PD1B160	P	G	L	A	A	A	Y	D	T	G	N	L	D	Y	16
PD1B162	P	G	L	A	A	A	Y	D	T	G	N	L	D	Y	16
PD1B164	P	G	L	A	A	A	Y	D	T	G	N	L	D	Y	16
PD1B11	P	G	L	A	A	A	Y	D	T	G	S	L	D	Y	17
PD1B183	P	G	L	A	A	A	Y	D	T	G	S	L	D	Y	17
PD1B184	P	G	L	A	A	A	Y	D	T	G	S	L	D	Y	17
PD1B185	P	G	L	A	A	A	Y	D	T	G	S	L	D	Y	17
PD1B187	P	G	L	A	A	A	Y	D	T	G	S	L	D	Y	17
PD1B194	P	G	L	A	A	A	Y	D	T	G	S	L	D	Y	17
PD1B195	P	G	L	A	A	A	Y	D	T	G	S	L	D	Y	17
PD1B196	P	G	L	A	A	A	Y	D	T	G	S	L	D	Y	17
HCDR3 genus 1	P	G	L	A	A	A	Y	D	T	G	X_6	L	D	Y	84

PD-1 mAb HCDR3 genus 1

PGLAAAYDTGX_6LDY (SEQ ID NO: 84),

wherein

X_6 is N or S.

Figure 9.

Antibody	HCDR3											
	Sequence											SEQ ID NO:
PD1B71	G	T	L	D	R	T	G	H	L	D	Y	18
PD1B177	G	T	L	D	R	T	G	H	L	D	Y	18
PD1B70	G	Y	V	R	A	T	G	M	L	D	Y	19
PD1B175	G	Y	V	R	A	T	G	M	L	D	Y	19
PD1B197	G	Y	V	R	A	T	G	M	L	D	Y	19
PD1B198	G	Y	V	R	A	T	G	M	L	D	Y	19
PD1B199	G	T	L	D	R	T	G	H	L	D	Y	18
PD1B200	G	T	L	D	R	T	G	H	L	D	Y	18
PD1B201	G	T	L	D	R	T	G	H	L	D	Y	18
HCDR3 genus 2	G	X_7	X_8	X_9	X_{10}	T	G	X_{11}	L	D	Y	85

PD-1 mAb HCDR3 genus 2

$GX_7X_8X_9X_{10}TGX_{11}LDY$ (SEQ ID NO; 85),

wherein

X_7 is T or Y;

X_8 is L or V;

X_9 is D or R;

X_{10} is R or A; and

X_{11} is H or M.

Figure 10.

Antibody	LCDR1											
	Sequence											SEQ ID NO:
PD1B114	R	A	S	Q	S	V	S	S	Y	L	A	20
PD1B149	R	A	S	Q	S	V	R	N	Y	L	A	21
PD1B160	R	A	S	Q	S	V	D	S	Y	L	A	22
PD1B162	R	A	S	Q	S	V	D	S	Y	L	A	22
PD1B164	R	A	S	Q	S	V	R	S	Y	L	A	23
PD1B11	R	A	S	Q	S	V	S	S	Y	L	A	20
PD1B183	R	A	S	Q	S	V	S	S	Y	L	A	20
PD1B184	R	A	S	Q	S	V	R	N	Y	L	A	21
PD1B185	R	A	S	Q	S	V	R	N	Y	L	A	21
PD1B187	R	A	S	Q	S	V	R	S	Y	L	A	23
PD1B71	R	A	S	Q	S	V	S	S	Y	L	A	20
PD1B177	R	A	S	Q	S	V	S	S	Y	L	A	20
PD1B70	R	A	S	Q	S	V	S	S	Y	L	A	20
PD1B175	R	A	S	Q	S	V	S	S	Y	L	A	20
PD1B194	R	A	S	Q	S	V	R	S	Y	L	A	23
PD1B195	R	A	S	Q	S	V	D	S	Y	L	A	22
PD1B196	R	A	S	Q	S	V	R	S	Y	L	A	23
PD1B197	R	A	S	Q	S	V	S	N	Y	L	A	24
PD1B198	R	A	S	Q	S	V	S	S	Y	L	A	20
PD1B199	R	A	S	Q	S	V	S	S	Y	L	A	20
PD1B200	R	A	S	Q	S	V	D	N	Y	L	A	25
PD1B201	R	A	S	Q	S	V	S	N	Y	L	A	24
LCDR1 genus	R	A	S	Q	S	V	X_{12}	X_{13}	Y	L	A	86

PD-1 mAb LCDR1 genus

RASQSV$X_{12}X_{13}$YLA (SEQ ID NO: 86),

wherein

X_{12} is S, R or D; and

X_{13} is S or N.

Figure 11.

Antibody	LCDR2							
	Sequence							SEQ ID NO:
PD1B114	D	A	S	N	R	A	T	26
PD1B149	D	A	S	N	R	A	T	26
PD1B160	D	A	S	D	R	A	T	27
PD1B162	D	A	S	N	R	A	T	26
PD1B164	D	A	S	Y	R	A	T	28
PD1B11	D	A	S	N	R	A	T	26
PD1B183	D	A	S	N	R	A	T	26
PD1B184	D	A	S	N	R	A	T	26
PD1B185	D	A	S	D	R	A	T	27
PD1B187	D	A	S	N	R	A	T	26
PD1B71	D	A	S	N	R	A	T	26
PD1B177	D	A	S	N	R	A	T	26
PD1B70	D	A	S	N	R	A	T	26
PD1B175	D	A	S	N	R	A	T	26
PD1B194	D	A	S	Y	R	A	T	28
PD1B195	D	A	S	N	R	A	T	26
PD1B196	D	A	S	N	R	A	T	26
PD1B197	D	A	S	N	R	A	T	26
PD1B198	D	A	S	S	R	A	T	29
PD1B199	D	A	S	T	R	A	T	30
PD1B200	D	A	S	N	R	A	T	26
PD1B201	D	A	S	N	R	A	T	26
LCDR2 genus	D	A	S	X_{14}	R	A	T	87

PD-1 mAb LCDR2 genus

$DASX_{14}RAT$ (SEQ ID NO: 87),

wherein

X_{14} is N, D, Y, S or T.

Figure 12.

Antibody	LCDR3									
	Sequence									SEQ ID NO:
PD1B114	Q	Q	R	S	N	W	P	L	T	31
PD1B149	Q	Q	R	N	Y	W	P	L	T	32
PD1B160	Q	Q	R	G	N	W	P	L	T	33
PD1B162	Q	Q	R	E	Y	W	P	L	T	34
PD1B164	Q	Q	R	D	Y	W	P	L	T	35
PD1B11	Q	Q	R	S	N	W	P	L	T	31
PD1B183	Q	Q	R	G	Y	W	P	L	T	36
PD1B184	Q	Q	R	N	Y	W	P	L	T	32
PD1B185	Q	Q	R	W	N	W	P	L	T	37
PD1B187	Q	Q	R	N	Y	W	P	L	T	32
PD1B71	Q	Q	R	S	N	W	P	L	T	31
PD1B177	Q	Q	R	S	N	W	P	L	T	31
PD1B70	Q	Q	R	S	N	W	P	L	T	31
PD1B175	Q	Q	R	S	N	W	P	L	T	31
PD1B194	Q	Q	R	D	Y	W	P	L	T	35
PD1B195	Q	Q	R	E	Y	W	P	L	T	34
PD1B196	Q	Q	R	N	Y	W	P	L	T	32
PD1B197	Q	Q	R	A	Y	W	P	L	T	38
PD1B198	Q	Q	R	A	E	W	P	L	T	39
PD1B199	Q	Q	R	N	Y	W	P	L	T	32
PD1B200	Q	Q	R	S	A	W	P	L	T	40
PD1B201	Q	Q	R	N	Y	W	P	L	T	32
LCDR3 genus	Q	Q	R	X_{15}	X_{16}	W	P	L	T	88

PD-1 mAb LCDR3 genus:

$QQRX_{15}X_{16}WPLT$ (SEQ ID NO: 88),

wherein

X_{15} is S, N, G, E, D, W, E or A; and

X_{16} is N, Y, E or A.

Figure 13.

mAb name	HCDR1						
	Sequence						SEQ ID NO:
TM3B103	N	Y	W	M	S		90
TM3B105	S	Y	A	M	S		91
TM3B109	S	Y	A	M	S		91
TM3B108	G	Y	W	M	H		92
TM3B113	D	Y	W	M	S		93
HCDR1 genus	X_{17}	Y	X_{18}	M	X_{19}		164

TIM3 mAb HCDR1 genus:

$X_{17}YX_{18}MX_{19}$ (SEQ ID NO: 164),

Wherein

X_{17} is N, S, G or D;

X_{18} is W or A; and

X_{19} is S or H.

Figure 14.

mAb	HCDR2																	
	Sequence																	SEQ ID NO:
TM3B103	A	I	S	G	S	G	G	S	T	Y	Y	A	D	S	V	K	G	99
TM3B105	A	I	S	G	S	G	G	S	T	Y	Y	A	D	S	V	K	G	99
TM3B109	A	I	S	G	S	G	G	S	T	Y	Y	A	D	S	V	K	G	99
TM3B108	A	I	S	Y	S	G	S	S	T	Y	Y	A	D	S	V	K	G	100
TM3B113	V	I	K	Y	S	G	G	S	K	Y	Y	A	D	S	V	K	G	101
HCDR2 genus	X_{20}	I	X_{21}	X_{22}	S	G	G	S	X_{23}	Y	Y	A	D	S	V	K	G	165

TIM-3 mAb HCDR2 genus

$X_{20}IX_{21}X_{22}SGGSX_{23}YYADSVKG$ (SEQ ID NO: 165),

wherein

X_{20} is A or V;

X_{21} is S or K;

X_{22} is G or Y; and

X_{23} is T or K.

Figure 15.

mAb	HCDR3										
	Sequence										SEQ ID NO:
TM3B103	D	H	W	D	P	N	F	L	D	Y	107
TM3B105	S	P	-	-	Y	A	P	L	D	Y	108
TM3B109	N	E	E	P	D	D	R	L	D	Y	109
TM3B108	G	T	N				W	L	D	Y	110
TM3B113	E	L	E			G	V	F	D	Y	111
HCDR3 genus	X_{24}	X_{25}	X_{26}	X_{27}	X_{28}	X_{29}	X_{30}	X_{31}	D	Y	166

$X_{24}X_{25}X_{26}X_{27}X_{28}X_{29}X_{30}X_{31}$DY (SEQ ID NO: 166),

wherein

X_{24} is D, S, N, G or E;

X_{25} is H, P, E, T or L;

X_{26} is W, E, N or deleted;

X_{27} is D, P or deleted;

X_{28} is P, Y, D or deleted;

X_{29} is N, A, D, G or deleted;

X_{30} is F, P, R, W or V; and

X_{31} is L or F.

Figue 16.

mAb	LCDR1																
	Sequence																SEQ ID NO:
TM3B103	R	A	S	Q	S	V	S	S	-					S	Y	L	A	117
TM3B105	R	A	S	Q	S	V	N	-						D	Y	L	A	118
TM3B109	K	S	S	Q	S	V	L	A	S	S	N	N	K	N	Y	L	A	119
TM3B108	R	A	S	Q	S	V	S	S						S	Y	L	A	117
TM3B113	R	A	S	Q	S	V	S	N						S	T	L	A	120
LCDR1 genus	X_{32}	X_{33}	S	Q	S	V	X_{34}	X_{35}	X_{36}	X_{37}	X_{38}	X_{39}	X_{40}	X_{41}	X_{42}	L	A	167

$X_{32}X_{33}SQSVX_{34}X_{35}X_{36}X_{37}X_{38}X_{39}X_{40}X_{41}X_{42}LA$ (SEQ ID NO: 167),

wherein

X_{32} is R or K;

X_{33} is A or S;

X_{34} is S, N or L;

X_{35} s S, A, N or deleted;

X_{36} is S or deleted;

X_{37} is S or deleted;

X_{38} is N or deleted;

X_{39} is N or deleted;

X_{40} is K or deleted;

X_{41} is S, D or N; and

X_{42} is Y or T.

Figure 17.

mAb	LCDR2							
	Sequence							SEQ ID NO:
TM3B103	G	A	S	S	R	A	T	126
TM3B105	D	A	S	N	R	A	T	127
TM3B109	W	A	S	T	R	E	S	128
TM3B108	G	A	S	S	R	A	T	126
TM3B113	T	A	S	S	R	A	T	129
LCDR2 genus	X_{43}	A	S	X_{44}	R	X_{45}	X_{46}	168

TIM-3 mAb LCDR2 genus

$X_{43}ASX_{44}RX_{45}X_{46}$ (SEQ ID NO: 168),

wherein

X_{43} is G, D, W or T;

X_{44} is S, N or T;

X_{45} is A or E; and

X_{46} is T or S.

Figure 18.

mAb	LCDR3									
	Sequence									SEQ ID NO:
TM3B103	Q	Q	Y	G	S	S	P	L	T	135
TM3B105	Q	Q	G	G	H	A	P	I	T	136
TM3B109	Q	Q	Y	Y	S	T	P	L	T	137
TM3B108	Q	Q	Y	G	S	S	P	L	T	138
TM3B113	Q	Q	S	Y	T	S	P	W	T	139
LCDR3 genus	Q	Q	X_{47}	X_{48}	X_{49}	X_{50}	P	X_{51}	T	169

$QQX_{47}X_{48}X_{49}X_{50}PX_{51}T$ (SEQ ID NO: 169),

wherein

X_{47} is Y, G or S;

X_{48} is G or Y;

X_{49} is S, H or T;

X_{50} is S, A or T; and

X_{51} is L, I or W.

Figure 19A.

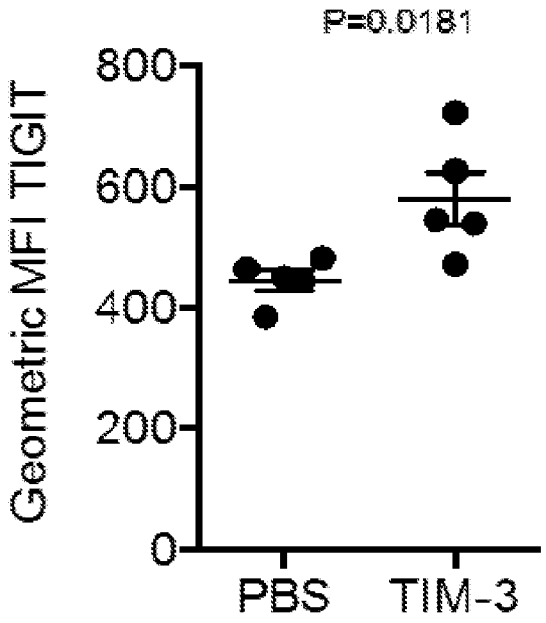


Figure 19B.

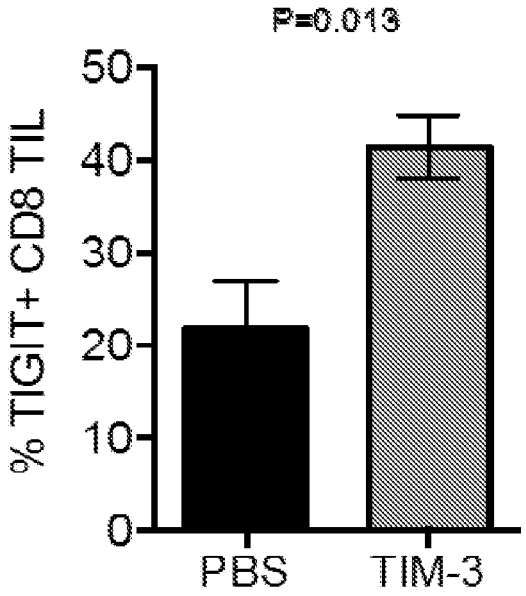


Figure 20A.

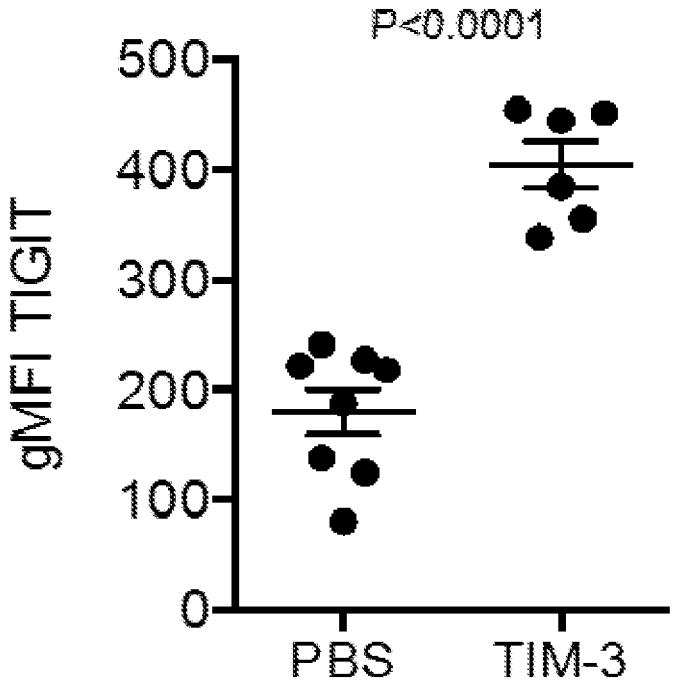


Figure 20B.

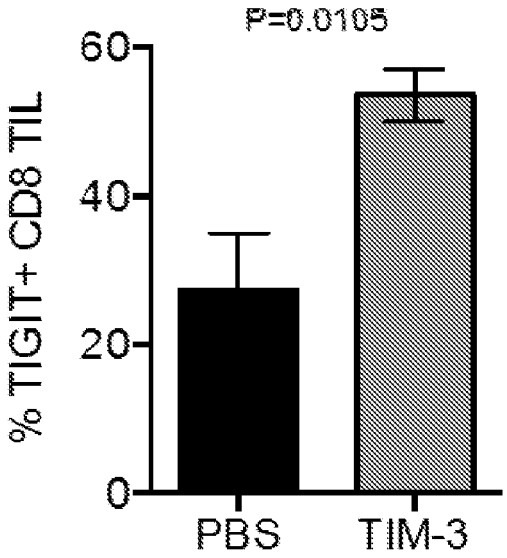


Figure 21.

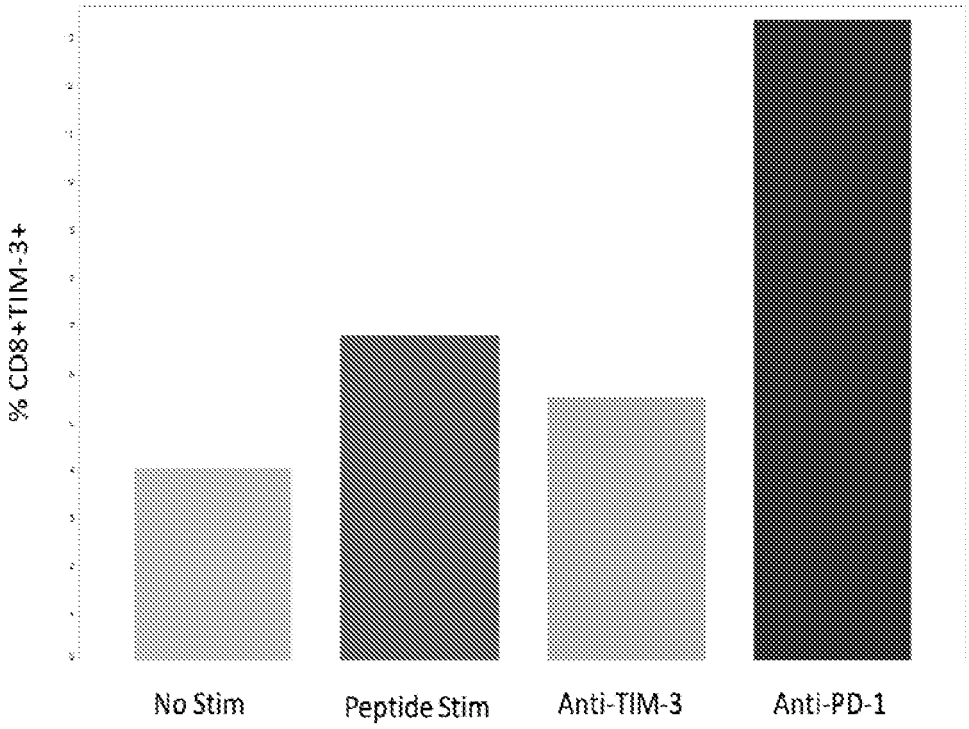


Figure 22A.

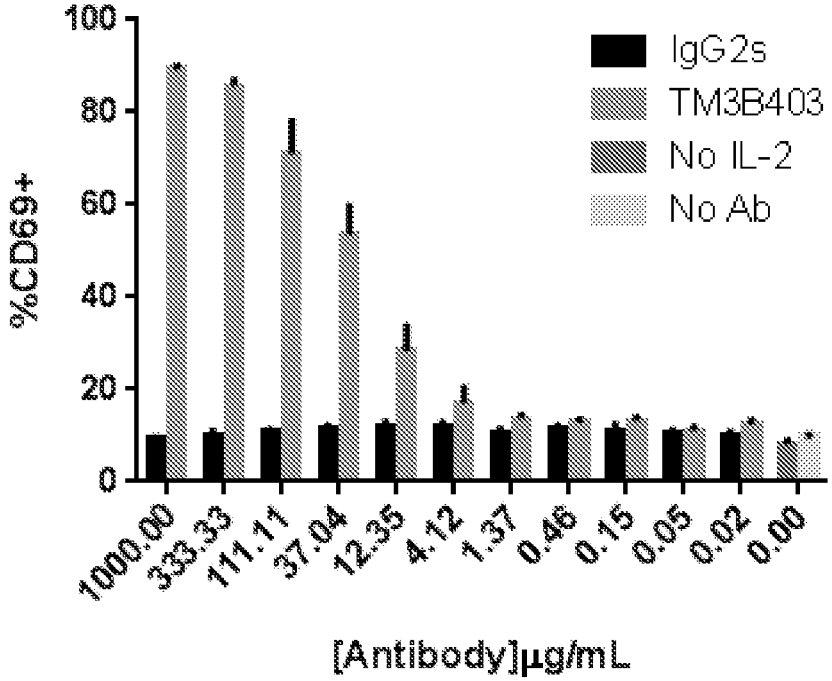
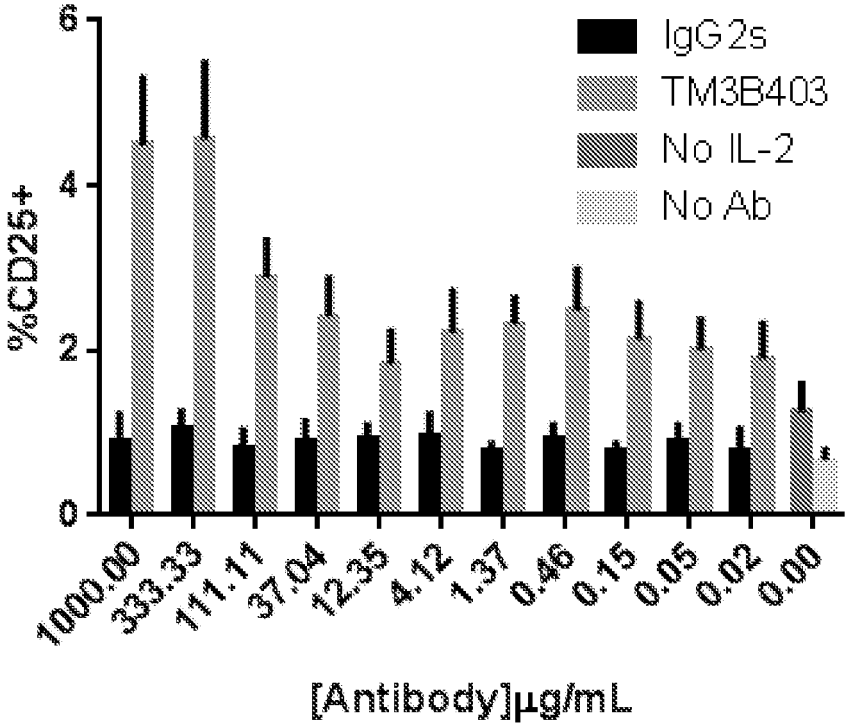

100
80
60
40
20
0
%CD69+
IgG2s
TM3B403
No IL-2
No Ab
1000.00
333.33
111.11
37.04
12.35
4.12
1.37
0.46
0.15
0.05
0.02
0.00
[Antibody]µg/mL

Figure 22B.


6
4
2
0
%CD25+
IgG2s
TM3B403
No IL-2
No Ab
1000.00
333.33
111.11
37.04
12.35
4.12
1.37
0.46
0.15
0.05
0.02
0.00
[Antibody]µg/mL